

Claims

1. A strain of *Francisella* species wherein a gene which encodes an enzyme in the purine pathway has been inactivated,
5 and which is able to produce a protective immune response in an animal, for use as a live prophylactic or therapeutic vaccine against infection by said *Francisella* species.
2. A strain according to claim 1 wherein the gene encodes an
10 enzyme, which is active early in the purine pathway.
3. A strain according to claim 1 wherein the gene is one of the first six enzymes in the purine pathway.
- 15 4. A strain according to claim 1, 2 or 3 wherein the gene is *purF*.
5. A strain according to any of claims 1 to 4 wherein said gene is inactivated by complete or partial deletion mutation or
20 by insertional mutation.
6. A strain according to any one of the preceding claims which is a strain of *Francisella tularensis*.
- 25 7. A strain according to claim 6 which is a strain of *Francisella tularensis* subspecies *tularensis*.
8. A strain according to claim 6 which is a strain of *Francisella tularensis* subspecies *novicida*.
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9. A pharmaceutical composition comprising a live strain of *Francisella* species wherein a gene, which encodes an enzyme in the purine pathway, has been inactivated, and which is able to produce a protective immune response in an animal, in
35 combination with a pharmaceutically acceptable carrier.

10. A composition according to claim 9 wherein the gene encodes an enzyme, which is active early in the purine pathway.

11. A composition according to claim 9 or 10 wherein the gene
5 is one of the first six enzymes in the purine pathway

12. A composition according to any of claims 9, 10 or 11 wherein the gene is *purF*.

10 13. A composition according to any of claims 9 to 12 wherein said gene is inactivated by complete or partial deletion mutation or by insertional mutation.

14. A pharmaceutical composition according to any one of claims
15 9 to 13 wherein the strain is a strain of *Francisella tularensis*.

15. A pharmaceutical composition according to claim 13 wherein
20 the strain is a strain of *Francisella tularensis* subspecies *tularensis* or a strain of *Francisella tularensis* subspecies *novicida*.

16. The use of a strain of *Francisella* species wherein a gene
25 which encodes an enzyme in the purine pathway has been inactivated, and which is able to produce a protective immune response in an animal, in the preparation of a live prophylactic or therapeutic vaccine against infection by said *Francisella* species.

30 17. The use according to claim 16 wherein the gene encodes an enzyme, which is active early in the purine pathway.

18. The use according to claim 16 or 17 wherein the gene is one
35 of the first six enzymes in the purine pathway

19. The use according to claim 16, 17 or 18 wherein the gene is *purF*.

20. The use according to claim any of claims 16 to 19 wherein
5 said gene is inactivated by complete or partial deletion
mutation or by insertional mutation.

21. The use according to any one of the preceding claims
wherein the strain is a strain of *Francisella tularensis*.
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22. The use according to claim 21 wherein the strain is a
strain of *Francisella tularensis* subspecies *tularensis* or a
strain of *Francisella tularensis* subspecies *novicida*.

15 23. A method of preventing or treating infection by a
Francisella species, which method comprises administering to an
animal an effective amount of a live strain according to any one
of claims 1 to 8 or a composition according to any one of claims
9 to 15.

20 24. A method according to claim 23 for preventing or treating
infection by *Francisella tularensis*, wherein the strain of
Francisella species used in the method is a strain of
Francisella tularensis subspecies *tularensis* or *Francisella*
25 *tularensis* subspecies *novicida*.

25. A method for preparing a strain according to any one of
claims 1 to 8, which comprises transforming a strain of
Francisella species so as to inactivate said gene using
30 cryotransformation.

26. A strain of *Francisella tularensis* subspecies *tularensis*
wherein a gene that encodes a *purA* gene has been inactivated.